Unit 3
Cell Metabolism

Chapter 7: Cellular Respiration and Fermentation

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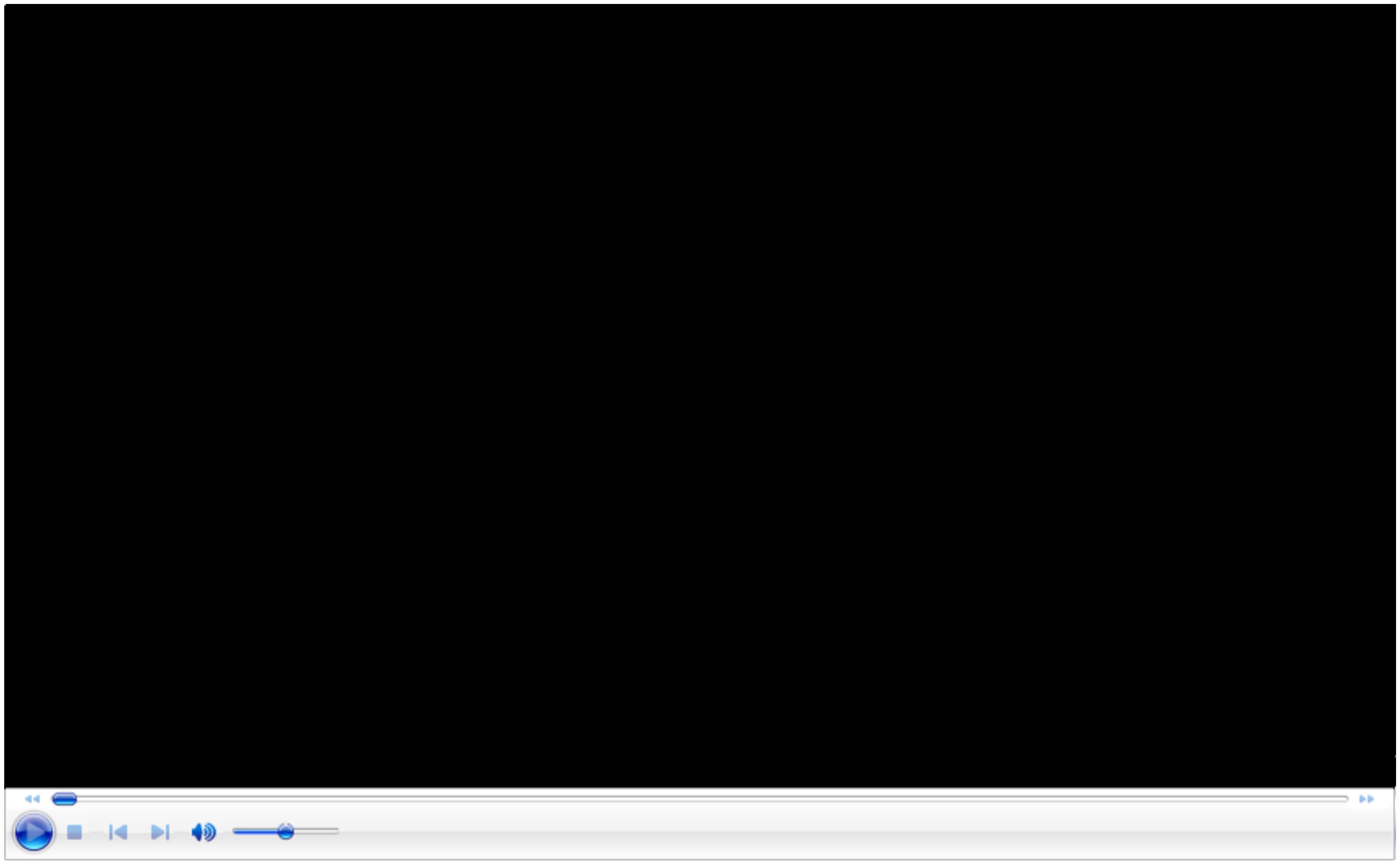
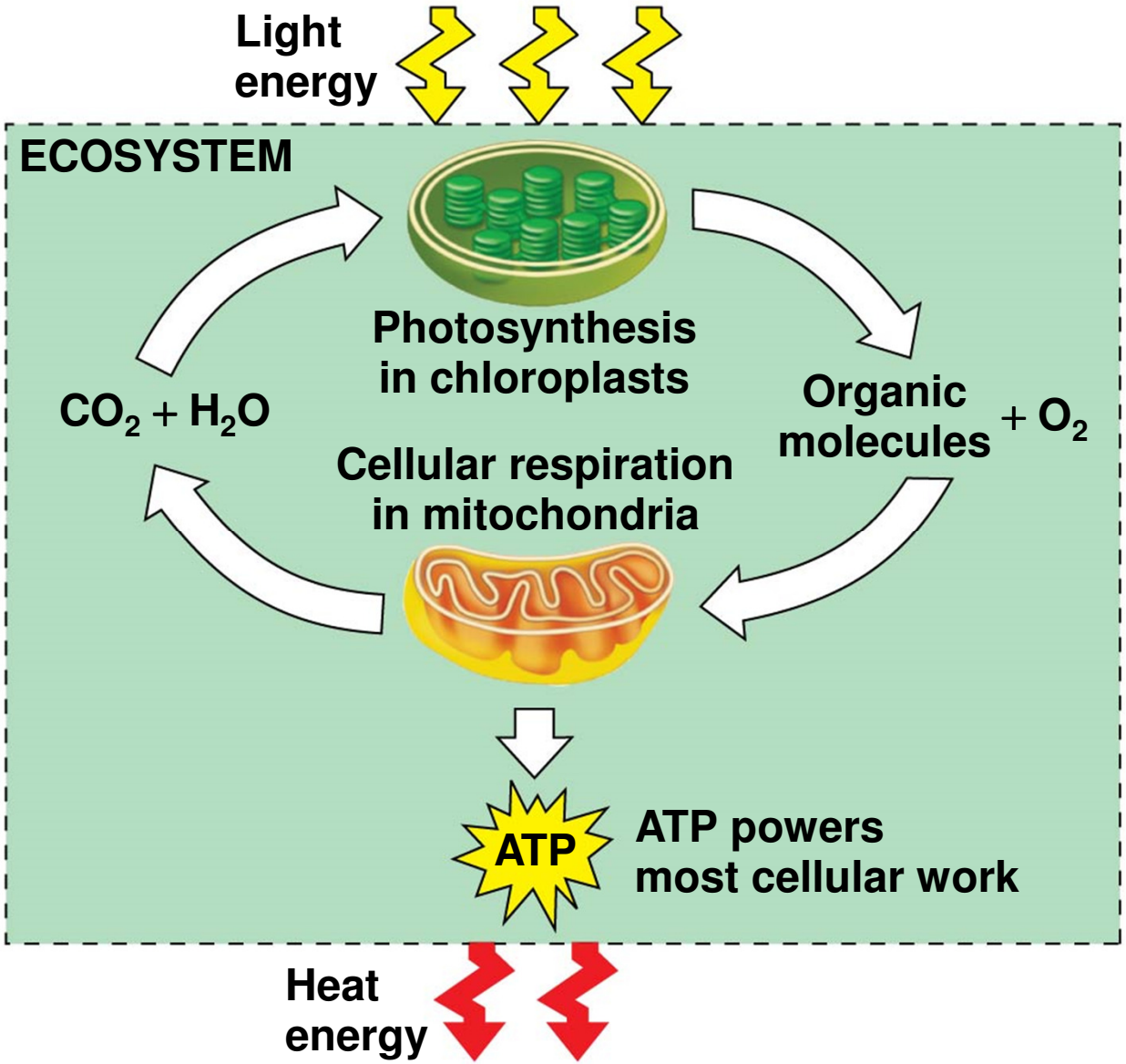
Overview: Life Is Work

- Living cells require energy from outside sources
- Energy flows into an ecosystem as sunlight and leaves as heat
  - Energy flows in a one-way direction
  - In contrast, the chemical elements essential to life are recycled
- Photosynthesis generates O_2 and organic molecules, which are used as fuel for cellular respiration
- Cells use chemical energy stored in organic molecules to regenerate ATP, which powers work



Video: Carbon Cycle

Figure 7.2


Light energy
ECOSYSTEM
Photosynthesis in chloroplasts
$CO_2 + H_2O$
Organic molecules $+ O_2$
Cellular respiration in mitochondria
ATP
ATP powers most cellular work
Heat energy

Concept 7.1: Catabolic pathways yield energy by oxidizing organic fuels

- The breakdown of organic molecules is exergonic
  - Some of the energy can be used to do work
  - Some is dissipated as heat
- **Fermentation** is a partial degradation of sugars that occurs without O_2
- **Aerobic respiration** consumes organic molecules and O_2 and yields ATP
  - Most effecient
- Anaerobic respiration is similar to aerobic respiration but consumes compounds other than O_2

- **Cellular respiration** includes both aerobic and anaerobic respiration but is often used to refer to aerobic respiration
- Although carbohydrates, fats, and proteins are all consumed as fuel, it is helpful to trace cellular respiration with the sugar glucose

$$C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \text{Energy (ATP + heat)}$$

  - Food = fuel
  - Catabolism is linked to work by a chemical drive shaft = ATP

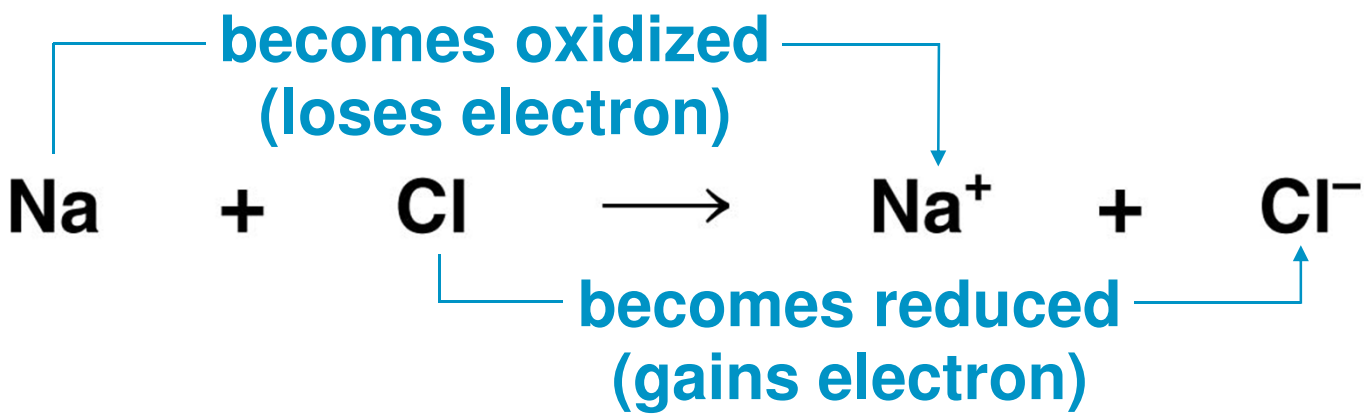
Redox Reactions: Oxidation and Reduction

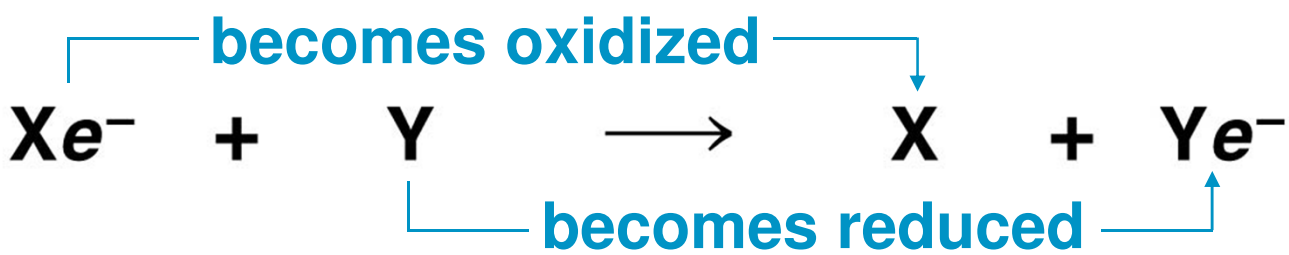
- The transfer of electrons during chemical reactions releases energy stored in organic molecules
- This released energy is ultimately used to synthesize ATP

The Principle of Redox

- Chemical reactions that transfer electrons between reactants are called oxidation-reduction reactions, or **redox reactions**
- In **oxidation**, a substance loses electrons, or is oxidized
- In **reduction**, a substance gains electrons, or is reduced
  - The amount of positive charge is reduced
- The electron donor is called the **reducing agent**
- The electron acceptor is called the **oxidizing agent**
- Redox reactions that move electrons closer to electronegative atoms, like oxygen, release chemical energy that can be put to work

Figure 7.UN01





Oxidation of Organic Fuel Molecules During Cellular Respiration

- During cellular respiration
  - Fuel (such as glucose) is oxidized
  - O_2 is reduced
- Organic molecules with an abundance of hydrogen, like carbohydrates and fats, are excellent fuels
- As hydrogen (with its electron) is transferred to oxygen, energy is released that can be used in ATP synthesis

becomes oxidized

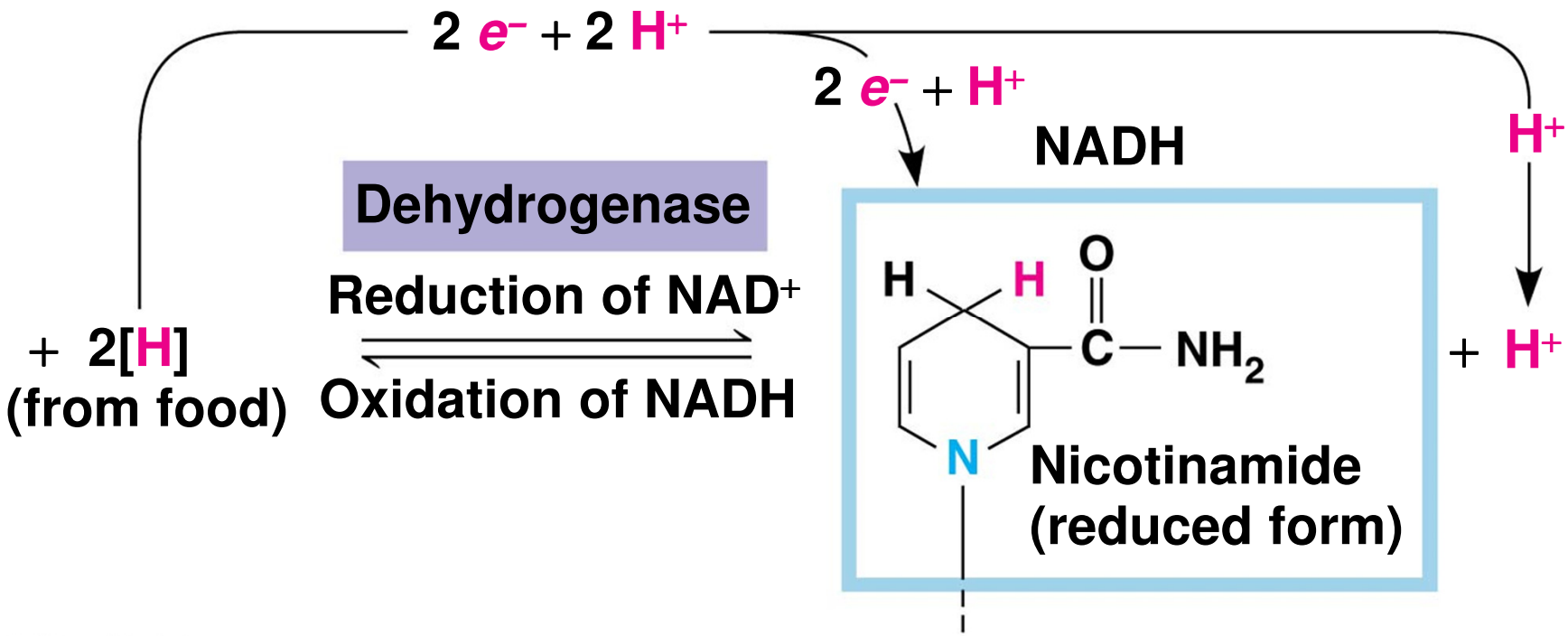
$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O + \text{Energy}$$

becomes reduced

Stepwise Energy Harvest via NAD^+ and the Electron Transport Chain

- In cellular respiration, glucose and other organic molecules are broken down in a series of steps
- Electrons from organic compounds are usually first transferred to a coenzyme called **NAD^+**
  - Electron carrier
- As an electron acceptor, NAD^+ functions as an oxidizing agent during cellular respiration
- Each NADH (the reduced form of NAD^+) represents stored energy that is tapped to synthesize ATP

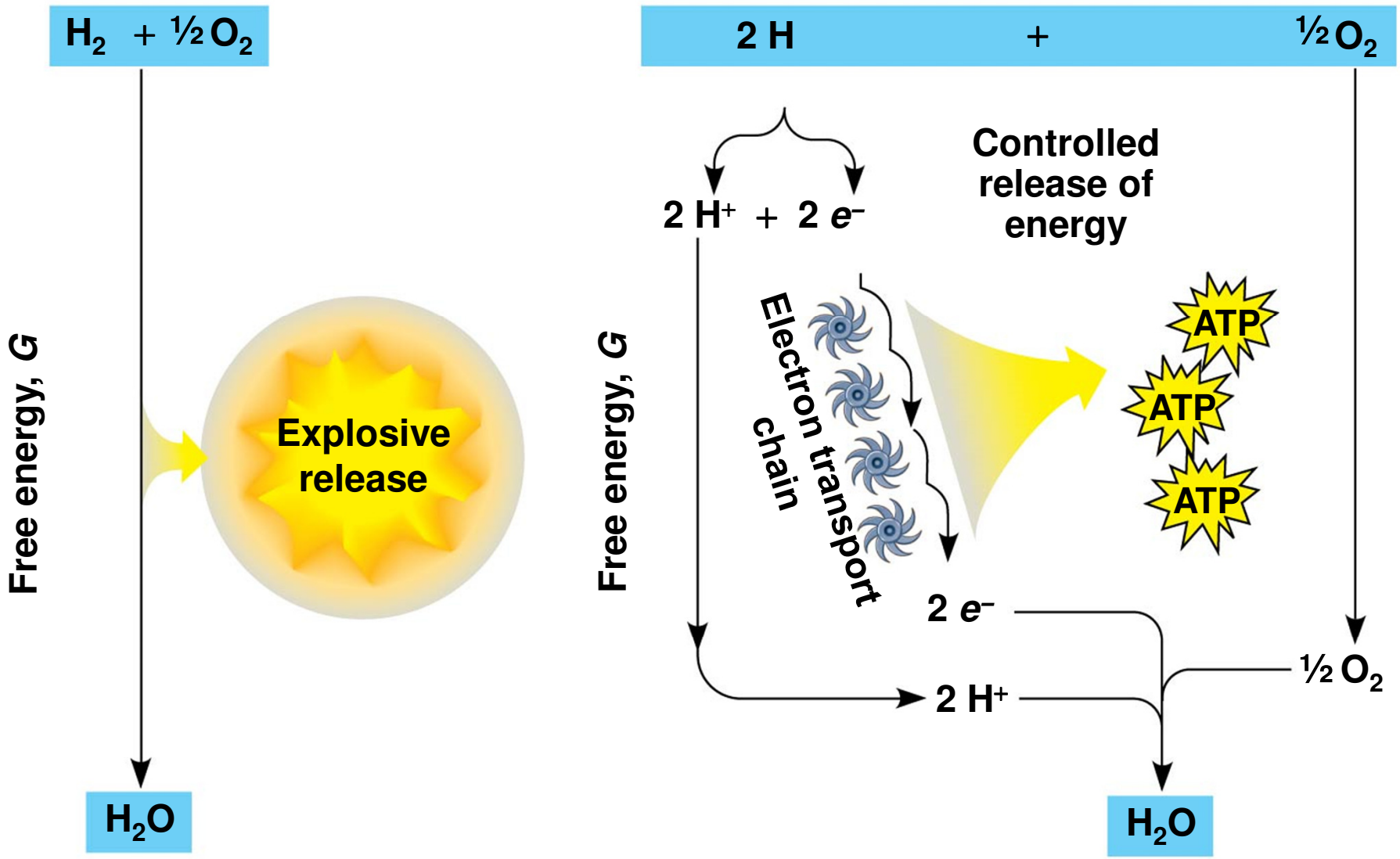
Figure 7.4b


2 e⁻ + 2 H⁺
2 e⁻ + H⁺
NADH
H⁺
Dehydrogenase
Reduction of NAD⁺
Oxidation of NADH
+ 2[H]
(from food)
H
H
O
C
NH2
N
+ H⁺
Nicotinamide
(reduced form)

H–C–OH + NAD⁺
Dehydrogenase
C=O + NADH + H⁺

- NADH passes the electrons to the **electron transport chain**
- Energy transfer from NADH to oxygen is exergonic
  - Unlike an uncontrolled reaction, the electron transport chain passes electrons in a series of steps instead of one explosive reaction
- O_2 pulls electrons down the chain in an energy-yielding tumble
- The energy yielded is used to regenerate ATP
- Glucose → NADH → electron transport chain → oxygen

Figure 7.5



(a) Uncontrolled reaction

(b) Cellular respiration

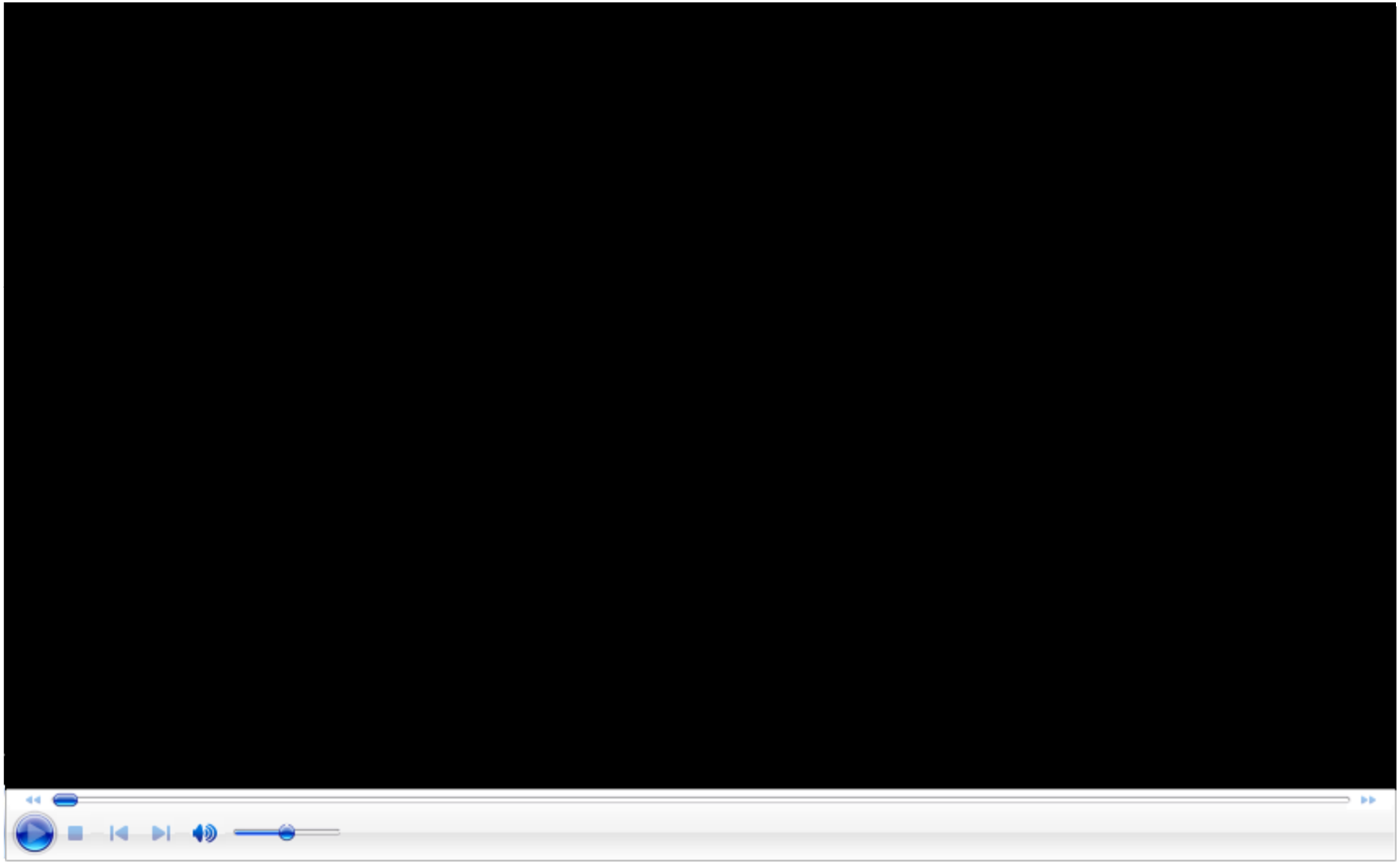
The Stages of Cellular Respiration: *A Preview*

- Harvesting of energy from glucose has three stages
  1. **Glycolysis**
     - Breaks down glucose into two molecules of pyruvate
     - Occurs in cytosol
  2. Pyruvate oxidation and the **citric acid cycle**
     - Completes the breakdown of glucose to carbon dioxide
     - Occurs in mitochondria of eukaryotes

3. **Oxidative phosphorylation**
   - Electron transport and chemiosmosis
     - Accounts for most of the ATP synthesis

- A smaller amount of ATP is formed in glycolysis and the citric acid cycle by **substrate-level phosphorylation**
  - An enzyme transfers a phosphate group from a substrate to ADP

- For each molecule of glucose degraded to CO_2 and water by respiration, the cell makes up to 32 molecules of ATP



Animation: Cellular Respiration
Right click slide / Select play

Figure 7.6-1

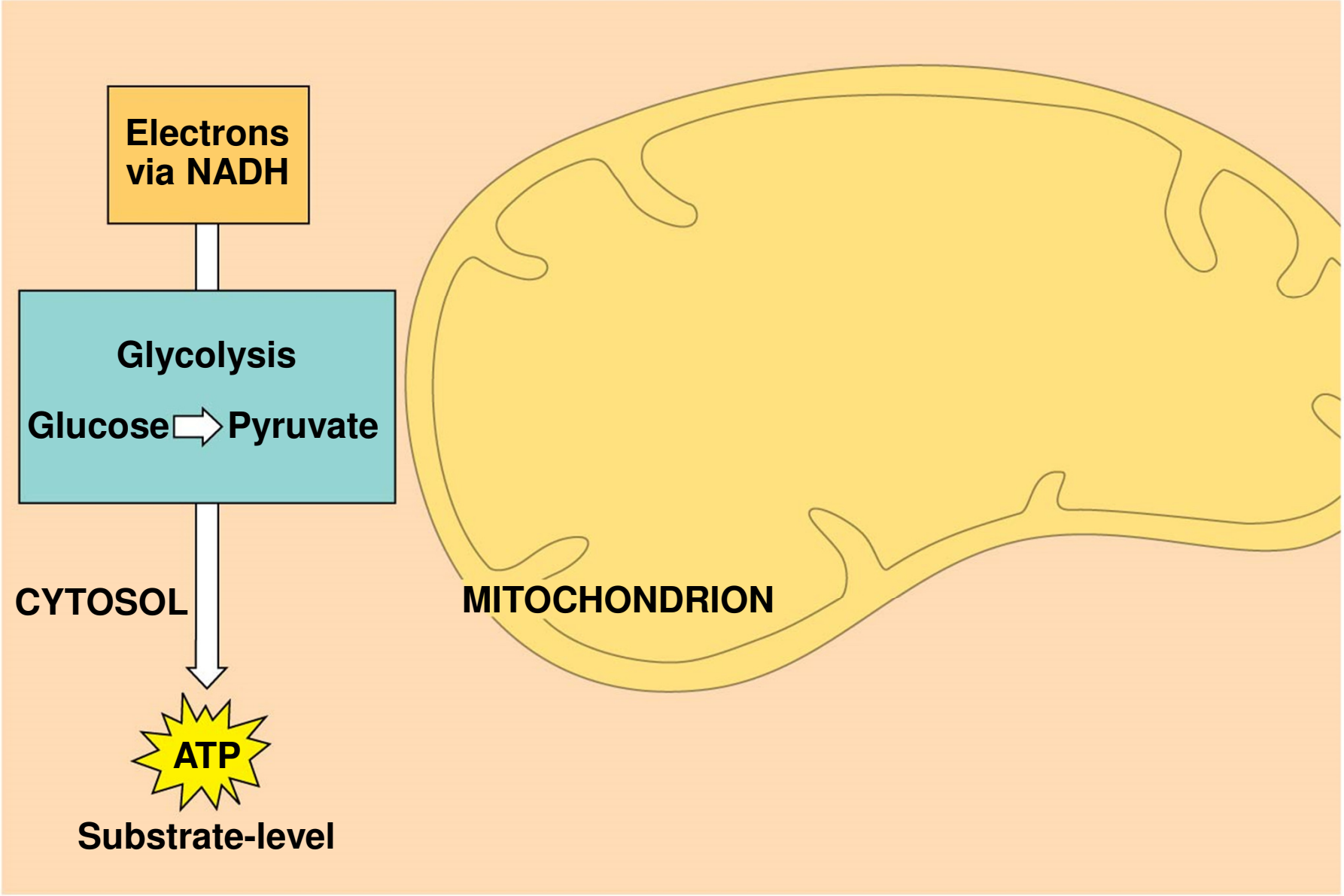

Electrons via NADH
Glycolysis
Glucose
Pyruvate
CYTOSOL
MITOCHONDRION
ATP
Substrate-level

Figure 7.6-2

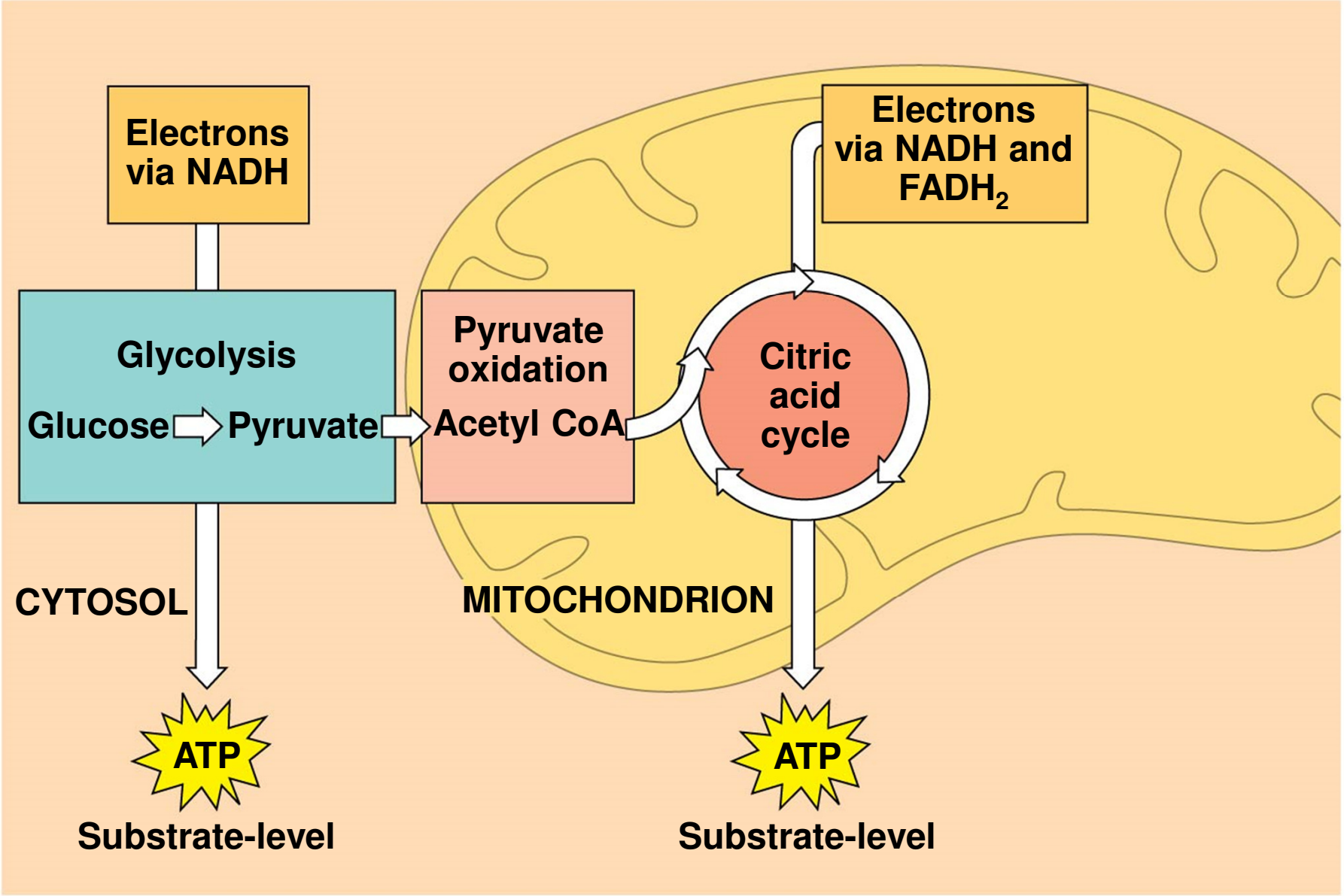

Electrons via NADH
Glycolysis
Glucose
Pyruvate
Pyruvate oxidation
Acetyl CoA
Citric acid cycle
Electrons via NADH and $FADH_2$
CYTOSOL
MITOCHONDRION
ATP
Substrate-level
ATP
Substrate-level

Figure 7.6-3

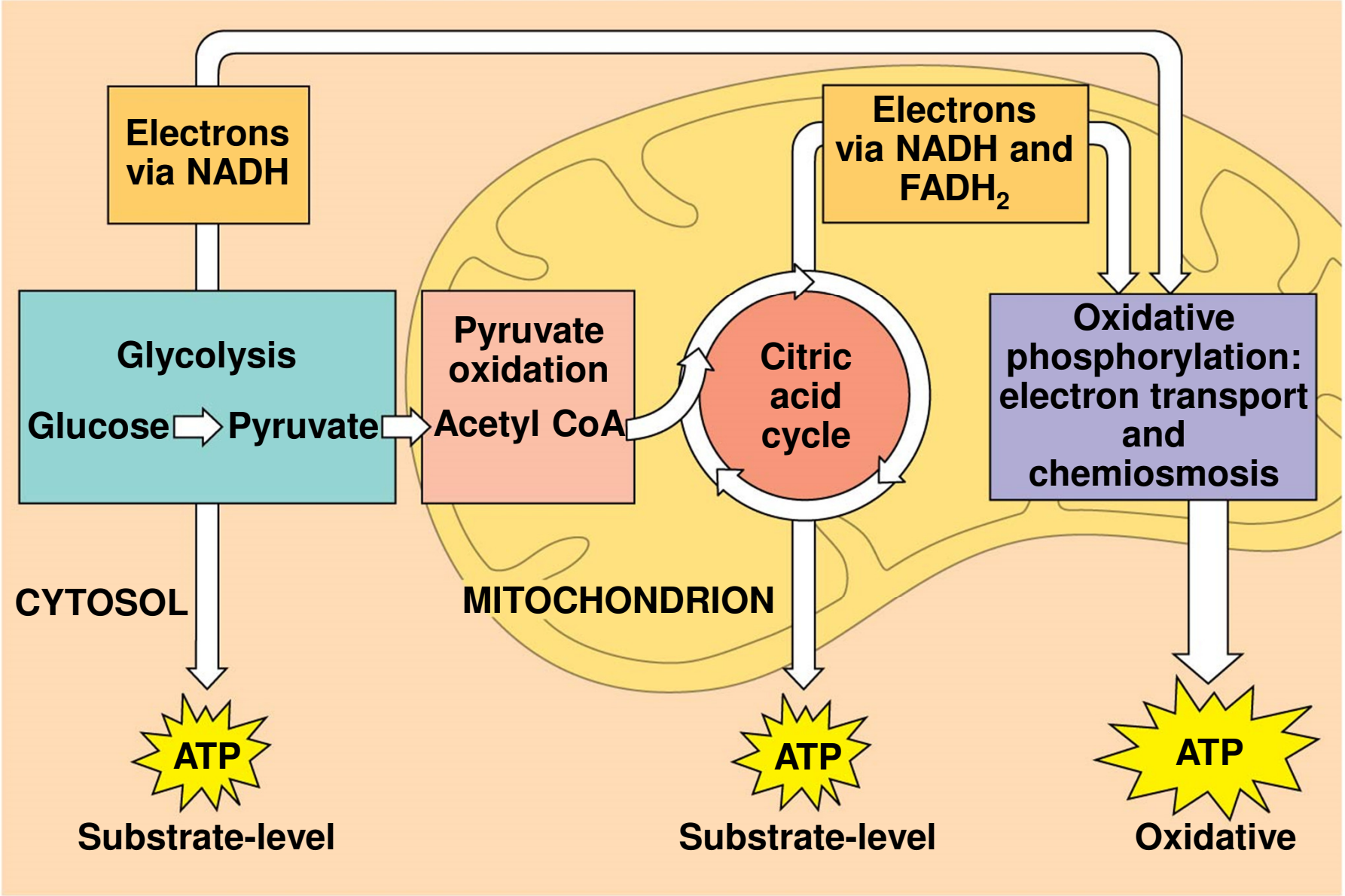
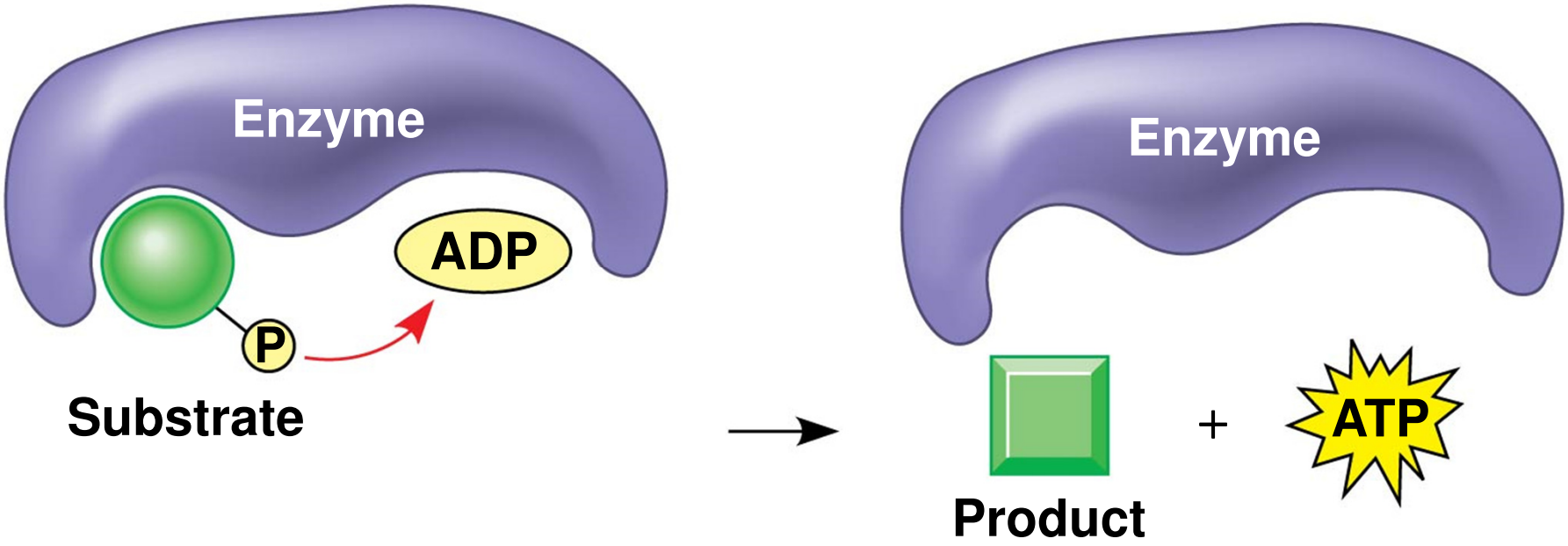

Electrons via NADH
Electrons via NADH and $FADH_2$
Glycolysis
Glucose
Pyruvate
Pyruvate oxidation
Acetyl CoA
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
CYTOSOL
MITOCHONDRION
ATP
ATP
ATP
Substrate-level
Substrate-level
Oxidative

Figure 7.7



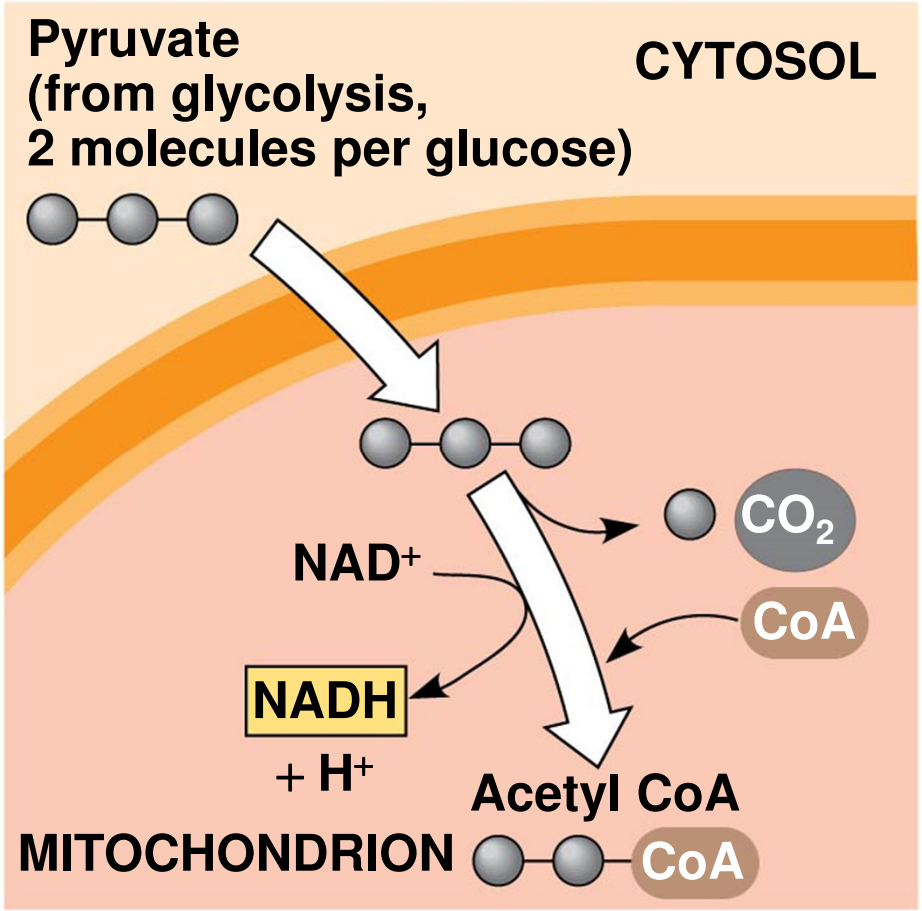
Concept 7.2: Glycolysis harvests chemical energy by oxidizing glucose to pyruvate

- Glycolysis ("sugar splitting") breaks down glucose into two molecules of pyruvate
  - Two 3-carbon sugars
- Occurs in the cytoplasm
- Has two major phases
  - Energy investment phase
    - 2 ATP used
  - Energy payoff phase
    - 4 ATP formed
    - 2 NADH result
- Glycolysis occurs whether or not O_2 is present!

Concept 7.3: After pyruvate is oxidized, the citric acid cycle completes the energy-yielding oxidation of organic molecules

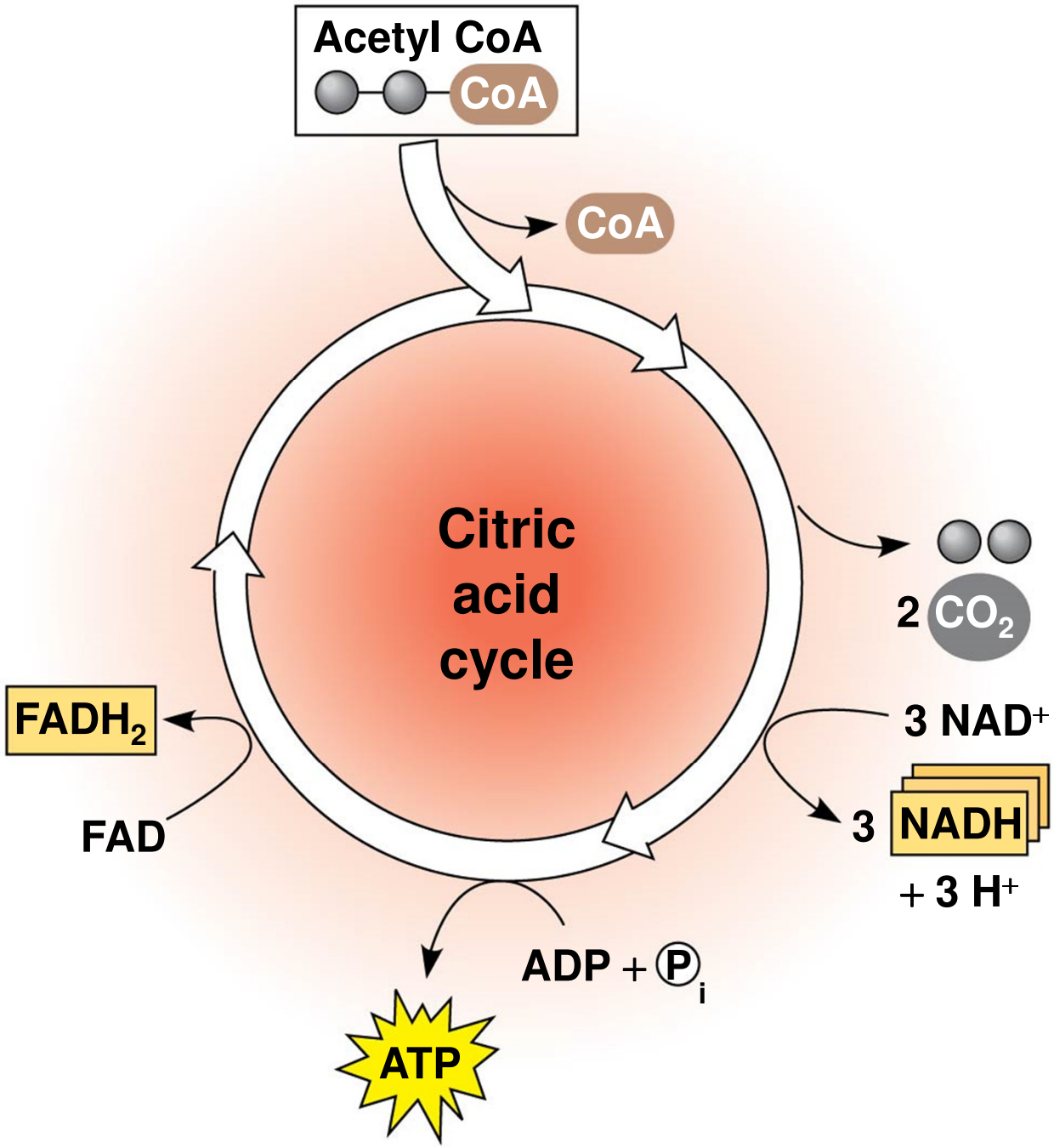
- In the presence of O_2
  - Pyruvate enters the mitochondrion (in eukaryotic cells), where the oxidation of glucose is completed
- Before the citric acid cycle can begin, pyruvate must be converted to acetyl coenzyme A (**acetyl CoA**), which links glycolysis to the citric acid cycle
- The citric acid cycle, also called the *Krebs cycle*, completes the breakdown of pyruvate to CO_2
  - Thus CO_2 is a waste product of respiration!
- The cycle oxidizes organic fuel derived from pyruvate

Figure 7.10a


Pyruvate
(from glycolysis,
2 molecules per glucose)
CYTOSOL
CO_2
NAD^+
CoA
NADH
$+ H^+$
Acetyl CoA
MITOCHONDRION
CoA

- Per turn, the citric acid cycle generates
  - 1 ATP
  - 3 NADH
  - 1 $FADH_2$
- Remember, glycolysis produced TWO pyruvate molecules
  - So for each glucose molecule entering respiration, multiply the numbers above by 2
- The NADH and $FADH_2$ produced by the cycle relay electrons extracted from food to the electron transport chain

Figure 7.10b


Acetyl CoA
CoA
CoA
Citric acid cycle
2 CO_2
3 NAD^+
3 NADH
+ 3 H^+
ADP + P_i
ATP
FAD
$FADH_2$

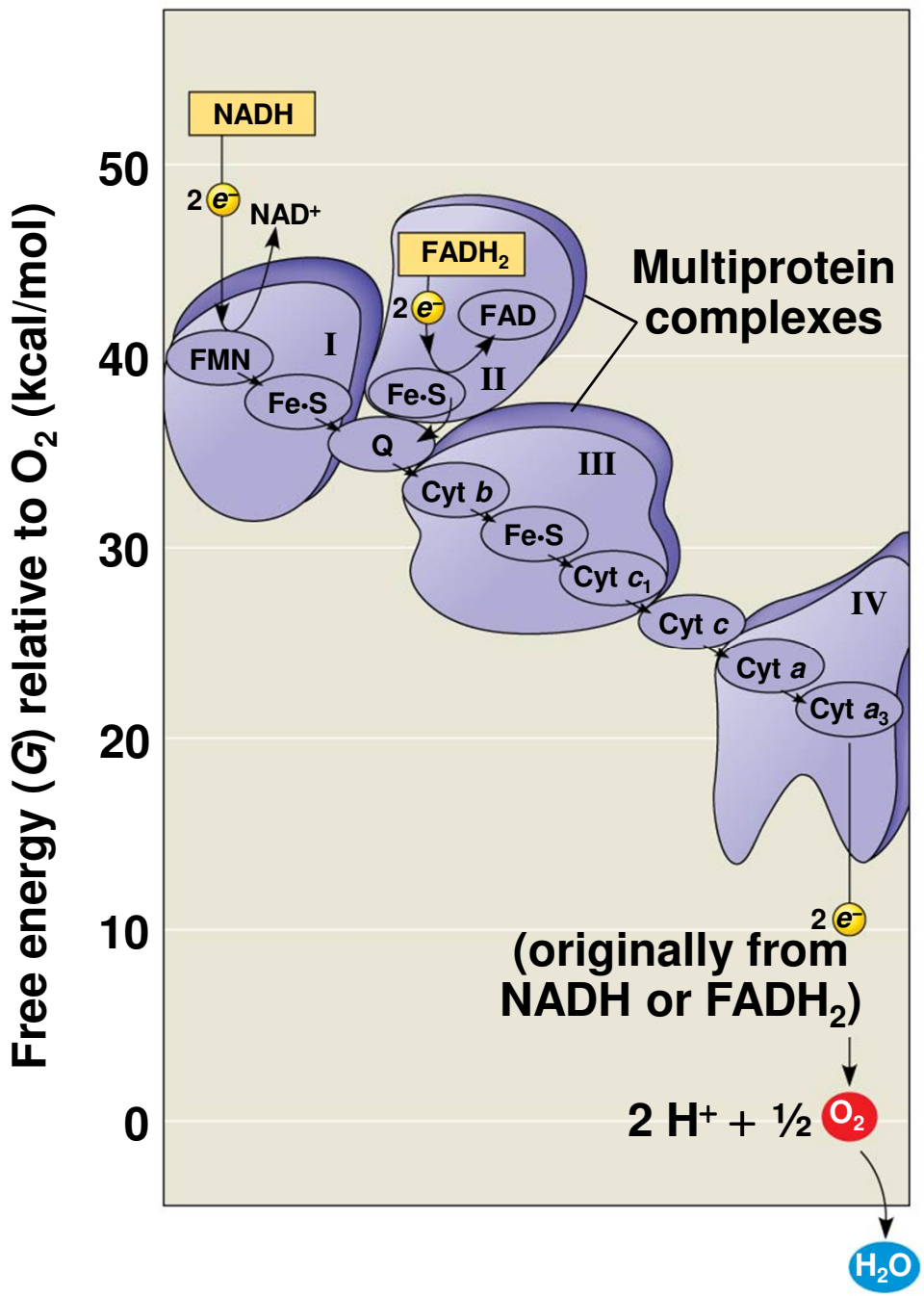
Concept 7.4: During oxidative phosphorylation, chemiosmosis couples electron transport to ATP synthesis

- So far only 4 ATP molecules per glucose molecule were produced by substrate-level phosphorylation
  - 2 net ATP from glycolysis
  - 2 ATP from citric acid cycle
- NADH and $FADH_2$ account for most of the energy extracted from food
- These two electron carriers donate electrons to the electron transport chain, which powers ATP synthesis via oxidative phosphorylation

The Pathway of Electron Transport

- The electron transport chain is in the inner membrane of the mitochondrion
  - In plasma membrane of prokaryotes
- Folding of membrane to form cristae increases surface area
  - More space for more chains!
- The carriers alternate reduced and oxidized states as they accept and donate electrons
- Electrons drop in free energy as they go down the chain and are finally passed to O_2, forming H_2O

Figure 7.12

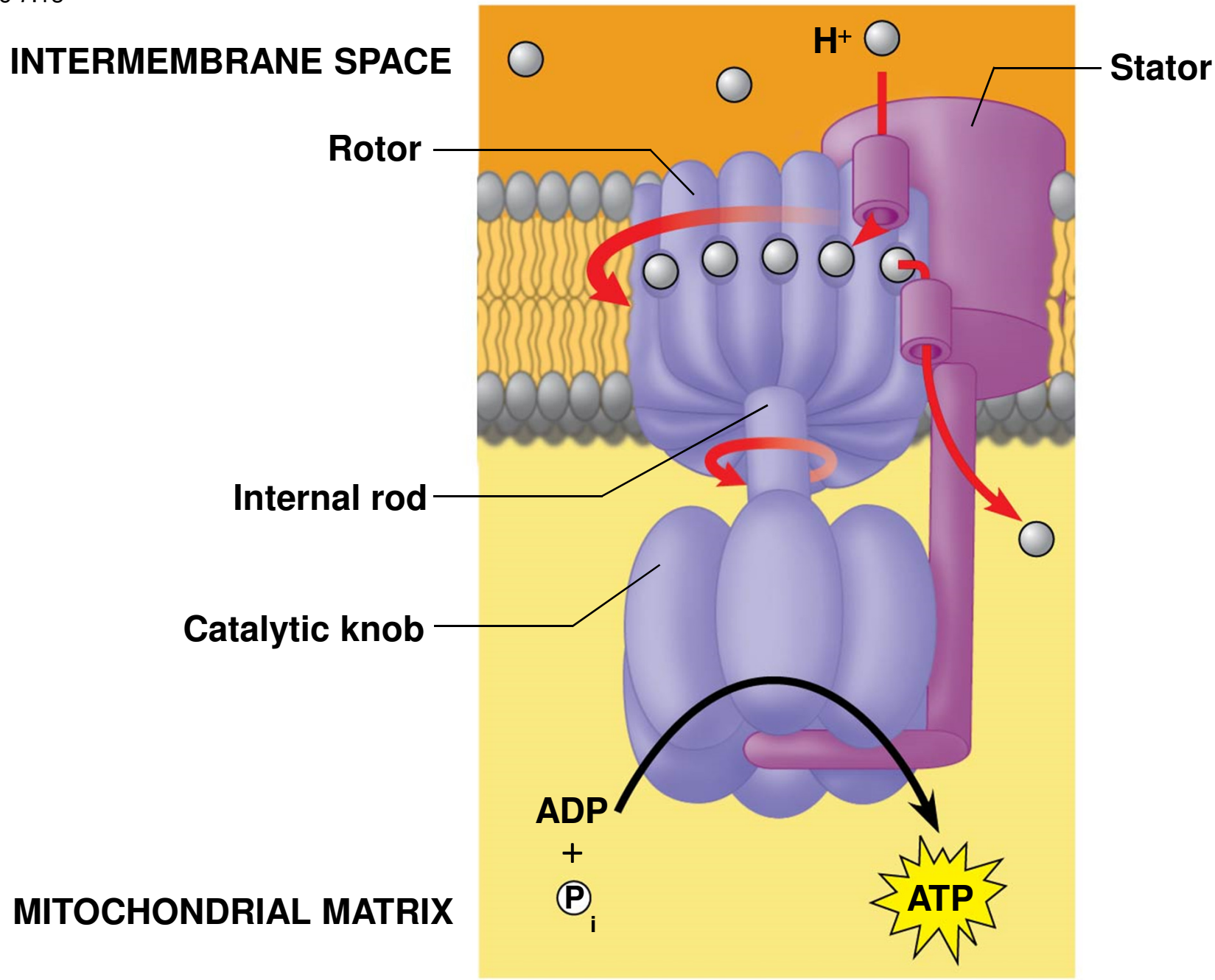

Free energy (G) relative to O2 (kcal/mol)
50
40
30
20
10
0
NADH
2 e⁻
NAD+
FMN
Fe•S
I
FADH2
2 e⁻
FAD
Fe•S
II
Q
Multiprotein complexes
III
Cyt b
Fe•S
Cyt c1
Cyt c
IV
Cyt a
Cyt a3
2 e⁻
(originally from NADH or FADH2)
2 H+ + ½ O2
H2O

- Electrons are transferred from NADH or $FADH_2$ to the electron transport chain
- Electrons are passed through a number of proteins including **cytochromes** (each with an iron atom) to O_2
- The electron transport chain generates no ATP directly
- It breaks the large free-energy drop from food to O_2 into smaller steps that release energy in manageable amounts

Chemiosmosis: The Energy-Coupling Mechanism

- Electron transfer in the electron transport chain causes proteins to pump H^+ from the mitochondrial matrix to the intermembrane space
- H^+ then moves back across the membrane, passing through the protein complex, **ATP synthase**
  - Uses the exergonic flow of H^+ to drive phosphorylation of ATP
    - IE-ATP synthase makes ATP from ADP and inorganic phosphate
- This is an example of **chemiosmosis**, the use of energy in a H^+ gradient to drive cellular work

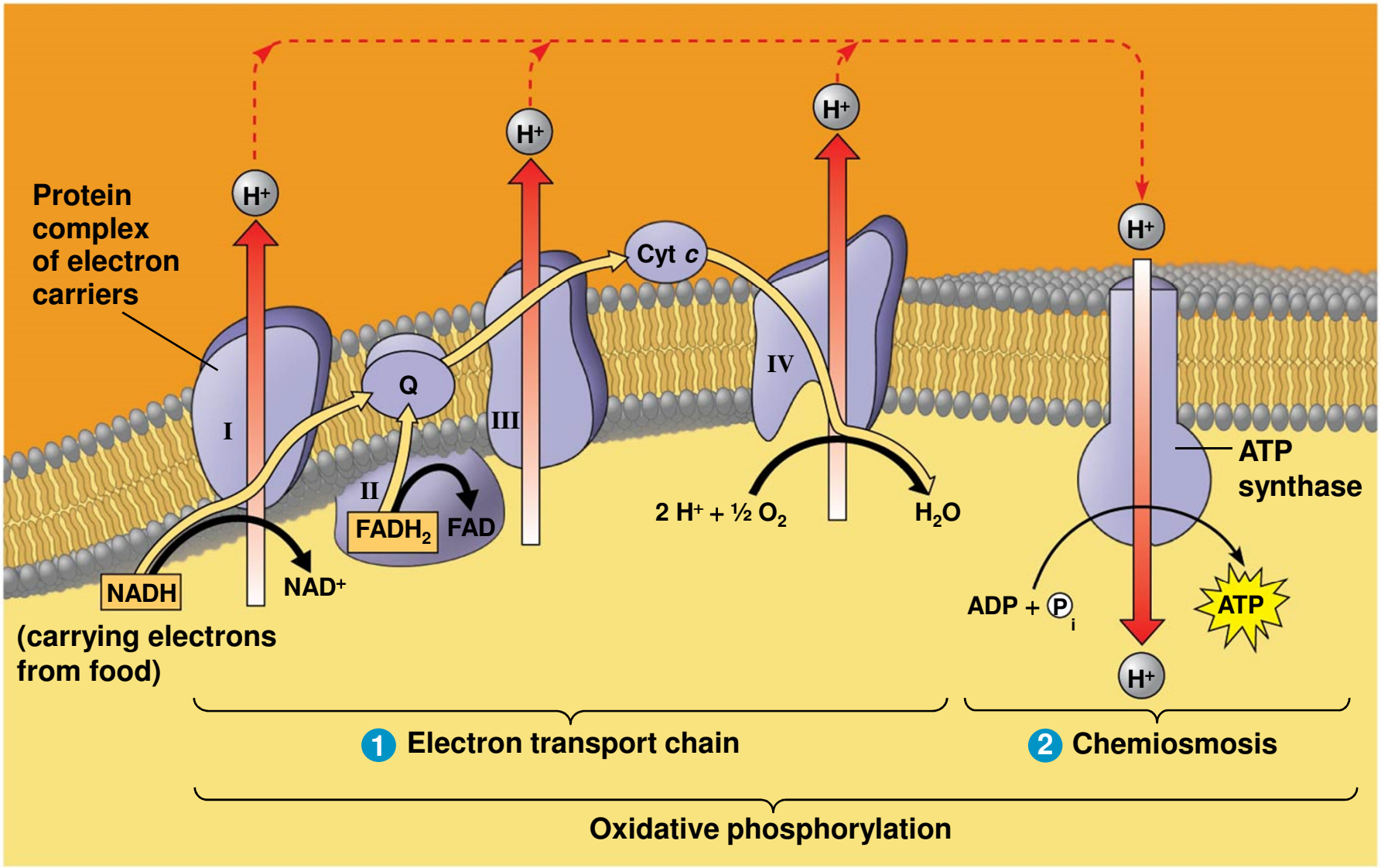
Figure 7.13


INTERMEMBRANE SPACE
H+
Stator
Rotor
Internal rod
Catalytic knob
ADP
+
Pi
ATP
MITOCHONDRIAL MATRIX

- The energy stored in a H^+ gradient across a membrane couples the redox reactions of the electron transport chain to ATP synthesis
- The H^+ gradient is referred to as a **proton-motive force**, emphasizing its capacity to do work

- Chemiosmosis is an energy-coupling mechanism that uses energy stored in the form of an H^+ gradient across a membrane to drive cellular work
  - Energy comes from exergonic redox reactions
  - Work performed is ATP synthesis

Figure 7.14


Protein complex of electron carriers
H+
H+
H+
H+
H+
Cyt c
I
II
III
IV
Q
FADH2
FAD
NADH
NAD+
(carrying electrons from food)
2 H+ + ½ O2
H2O
ATP synthase
ADP + Pi
ATP
1 Electron transport chain
2 Chemiosmosis
Oxidative phosphorylation

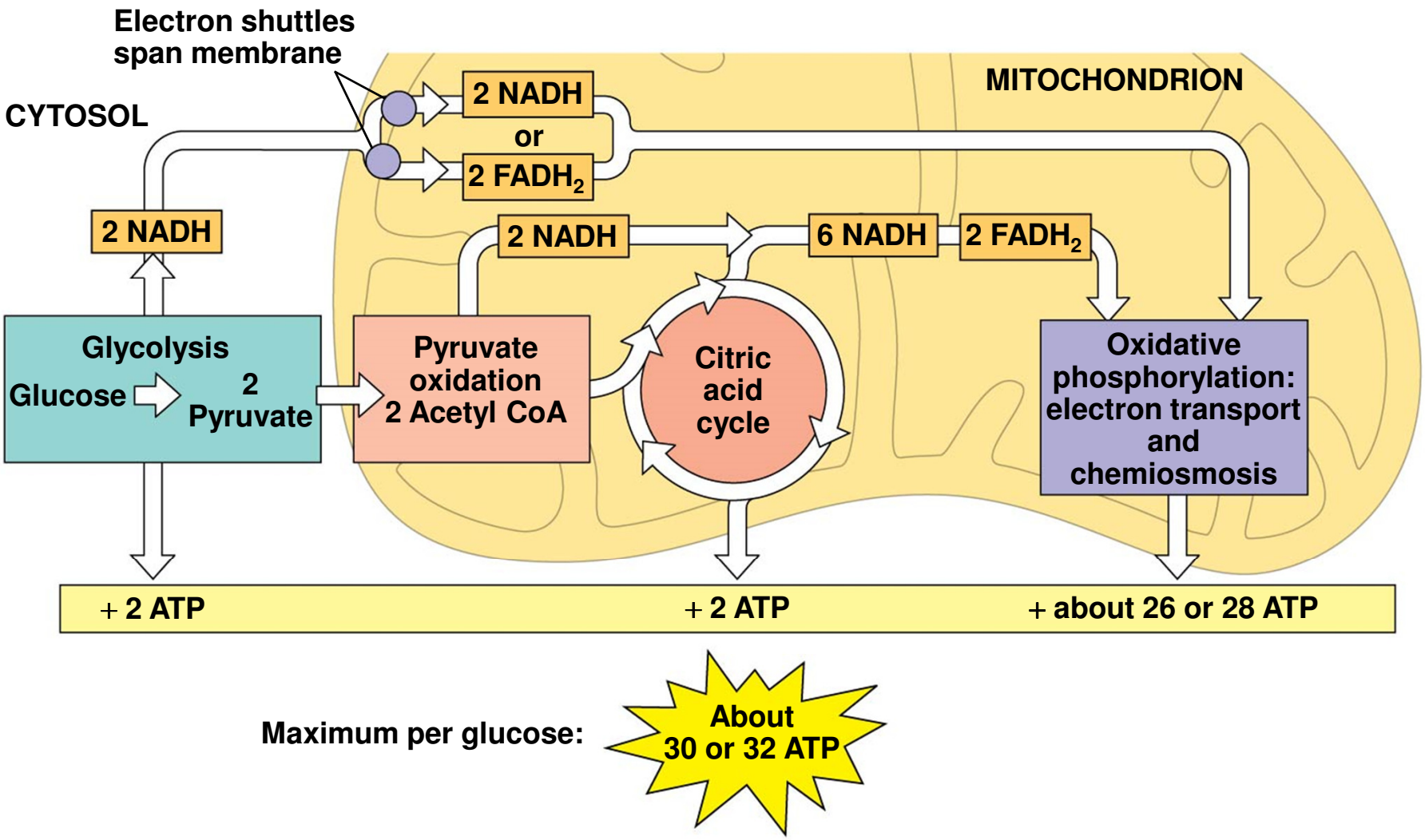
An Accounting of ATP Production by Cellular Respiration

- During cellular respiration, most energy flows in the following sequence:

  glucose $\rightarrow$ NADH $\rightarrow$ electron transport chain $\rightarrow$ proton-motive force $\rightarrow$ ATP

- Total yield of about 32 ATP during respiration
  - Also produces six molecules of CO_2

Figure 7.15

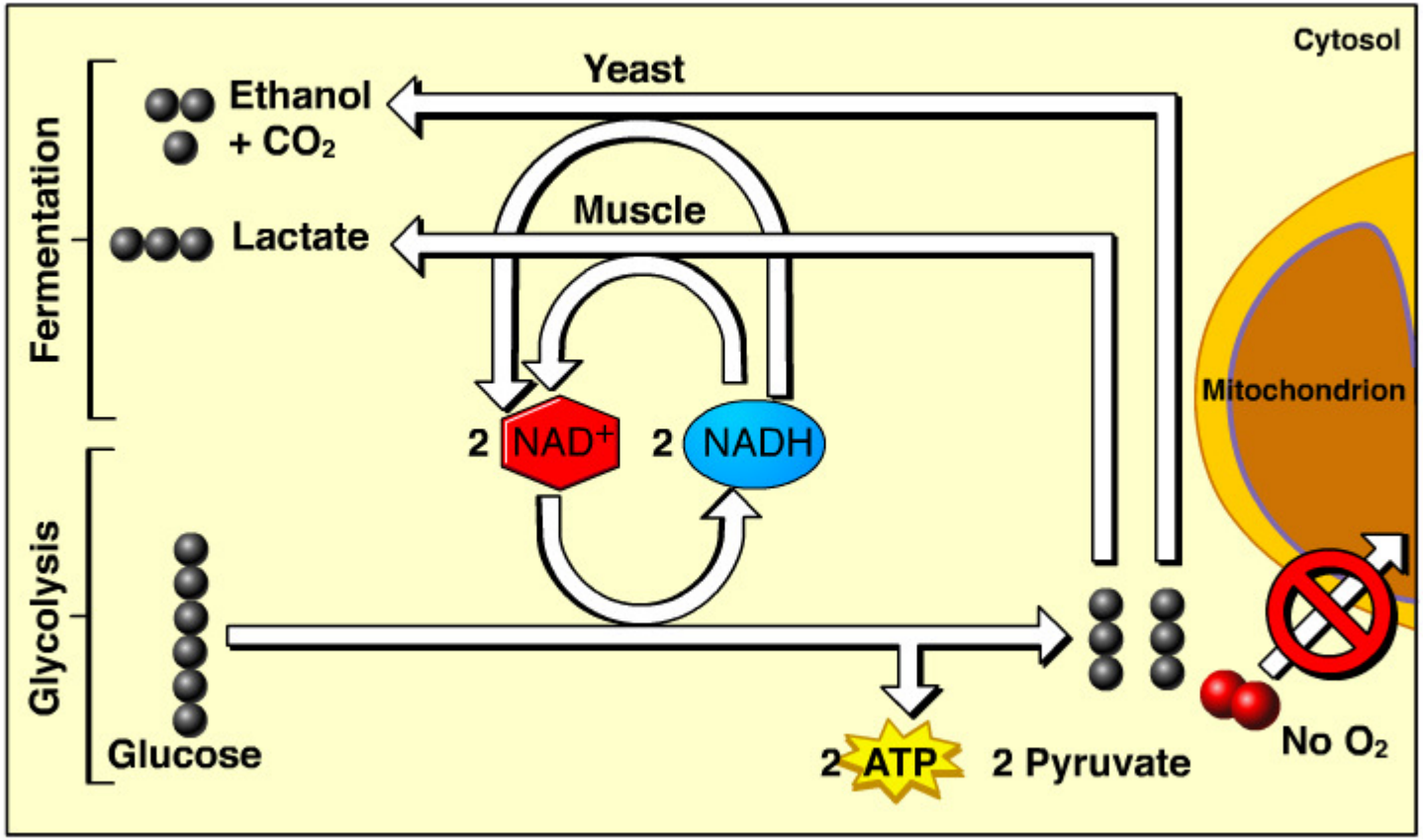

Electron shuttles span membrane
CYTOSOL
MITOCHONDRION
2 NADH
or
2 FADH2
2 NADH
2 NADH
6 NADH
2 FADH2
Glycolysis
Glucose
2 Pyruvate
Pyruvate oxidation
2 Acetyl CoA
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
+ 2 ATP
+ 2 ATP
+ about 26 or 28 ATP
Maximum per glucose:
About 30 or 32 ATP

Concept 7.5: Fermentation and anaerobic respiration enable cells to produce ATP without the use of oxygen

- Most cellular respiration requires O_2 to produce ATP
- Without O_2, the electron transport chain will cease to operate
- In that case, glycolysis couples with fermentation or anaerobic respiration to produce ATP
  - Anaerobic respiration uses an electron transport chain with a final electron acceptor other than O_2
  - Fermentation uses substrate-level phosphorylation instead of an electron transport chain to generate ATP

Types of Fermentation

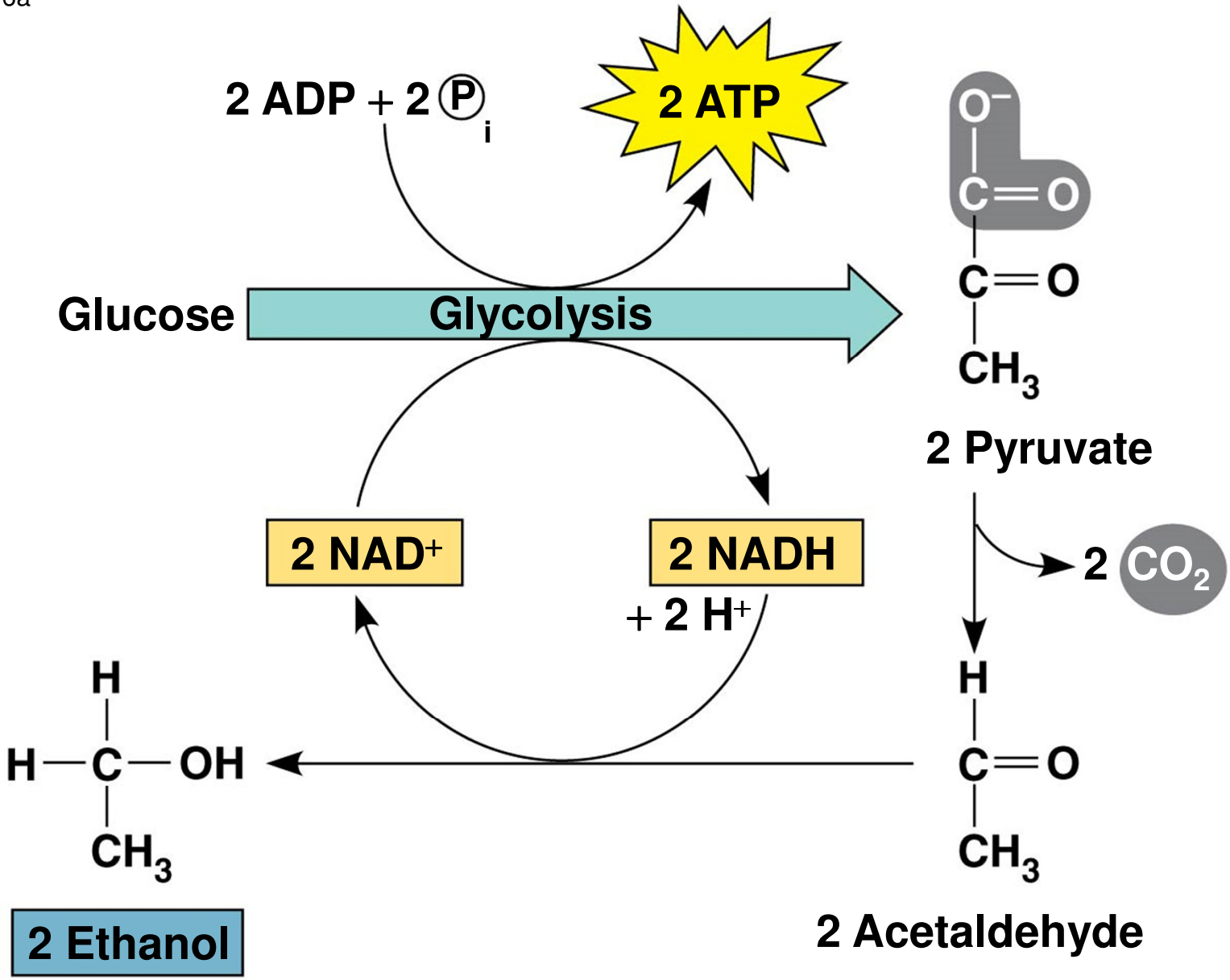
- Fermentation consists of glycolysis plus reactions that regenerate NAD^+, which can be reused by glycolysis
  - Remember, glycolysis generates 2 net ATP whether or not oxygen is present
- Two common types
  - Alcohol fermentation
  - Lactic acid fermentation



Animation: Fermentation Overview
Right click slide / Select play

- In **alcohol fermentation**, pyruvate is converted to ethanol in two steps
  - The first step releases CO_2 from pyruvate
  - The second step reduces acetaldehyde to ethanol
- Alcohol fermentation by yeast is used in brewing, winemaking, and baking

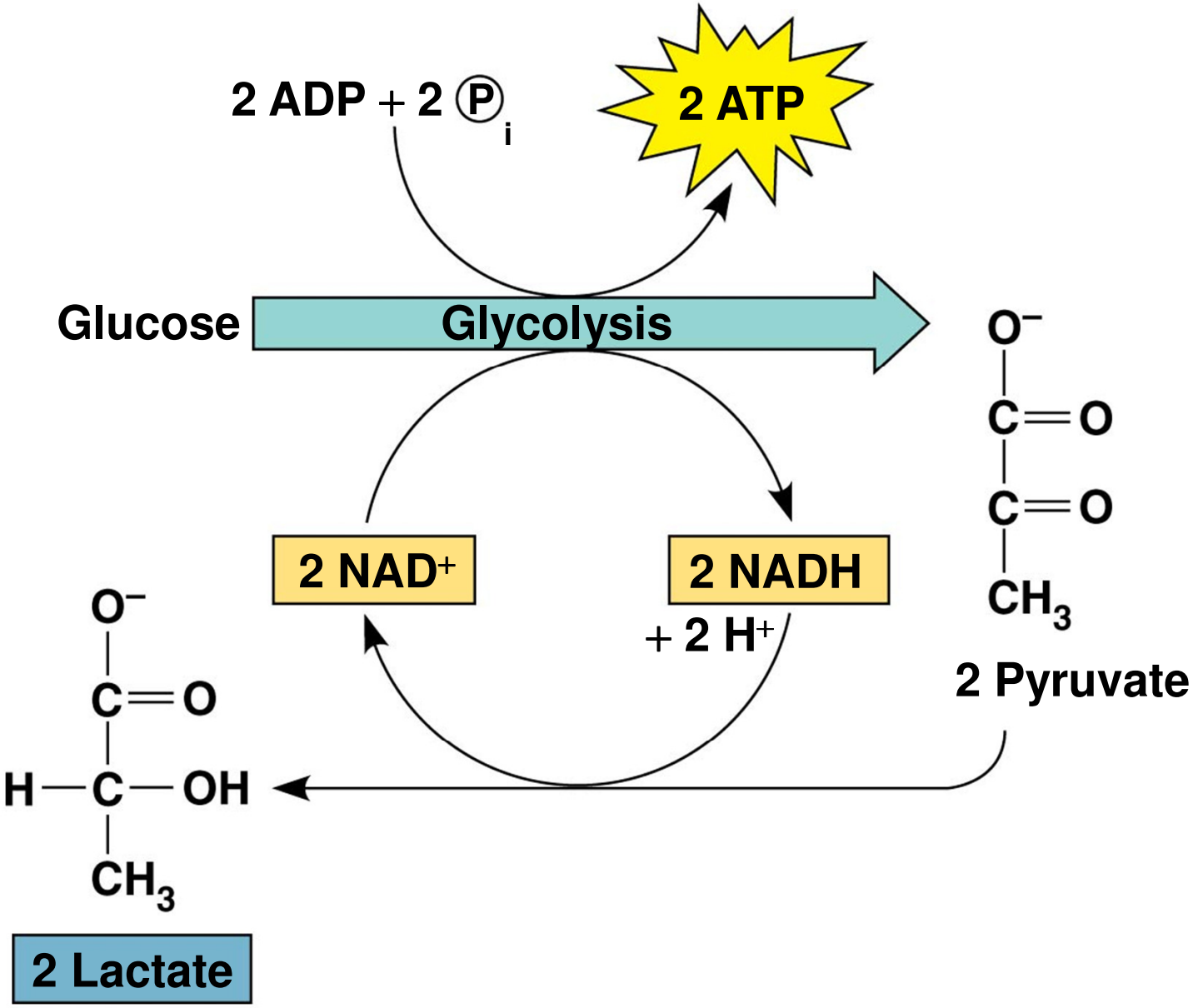
Figure 7.16a



(a) Alcohol fermentation

- In **lactic acid fermentation**, pyruvate is reduced by NADH, forming <u>lactate</u> as an end product
  - NO release of CO_2!
- Lactic acid fermentation by some fungi and bacteria is used to make cheese and yogurt
- Human muscle cells use lactic acid fermentation to generate ATP when O_2 is scarce
  - During strenuous exercise

Figure 7.16b



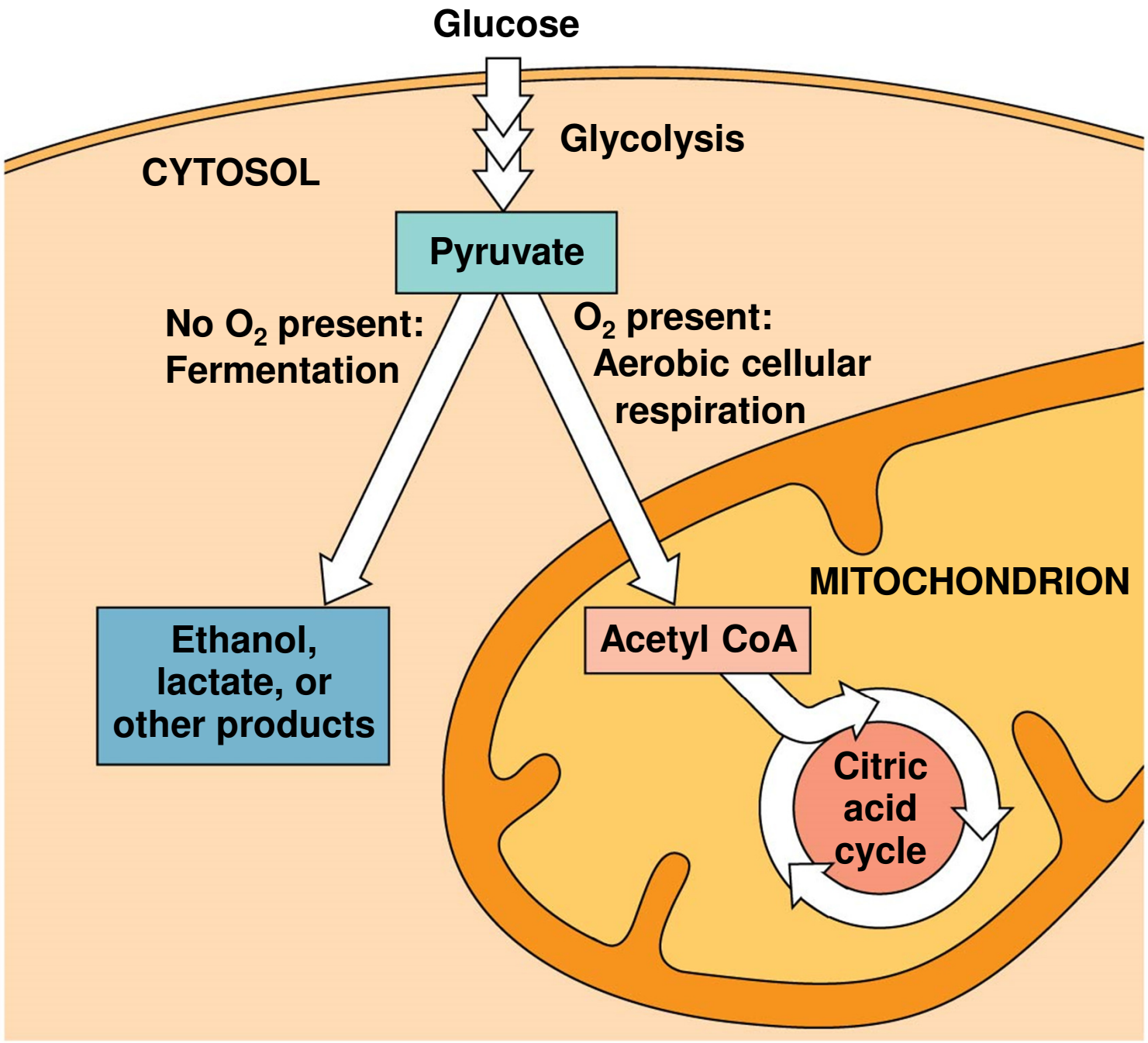
(b) Lactic acid fermentation

Comparing Fermentation with Anaerobic and Aerobic Respiration

- All use glycolysis (net ATP = 2) to oxidize glucose and harvest chemical energy of food
- In all three, NAD^+ is the oxidizing agent that accepts electrons during glycolysis
- The processes have different final electron acceptors:
  - An organic molecule (such as pyruvate or acetaldehyde) in fermentation
  - O_2 in cellular respiration
- Different amounts of ATP produced
  - Cellular respiration produces 32 ATP per glucose
  - Fermentation produces 2 ATP per glucose

- **Obligate anaerobes** carry out only fermentation or anaerobic respiration
  - Cannot survive in the presence of O_2!
- Yeast and many bacteria are **facultative anaerobes**
  - They can survive using either fermentation or cellular respiration
- Our muscle cells behave as facultative anaerobes
  - Pyruvate is a fork in the metabolic road that leads to two alternative catabolic routes

Figure 7.17


Glucose
Glycolysis
CYTOSOL
Pyruvate
No O_2 present:
Fermentation
O_2 present:
Aerobic cellular
respiration
MITOCHONDRION
Ethanol,
lactate, or
other products
Acetyl CoA
Citric
acid
cycle

The Evolutionary Significance of Glycolysis

- Ancient prokaryotes are thought to have used glycolysis long before there was oxygen in the atmosphere
- Very little O_2 was available in the atmosphere until about 2.7 billion years ago, so early prokaryotes likely used only glycolysis to generate ATP
- Glycolysis is a very ancient process

Concept 7.6: Glycolysis and the citric acid cycle connect to many other metabolic pathways

- Catabolic pathways funnel electrons from many kinds of organic molecules into cellular respiration
- Glycolysis accepts a wide range of carbohydrates
- Proteins must be digested to amino acids and amino groups must be removed before amino acids can feed glycolysis or the citric acid cycle
- Fats are digested to glycerol (used in glycolysis) and fatty acids
- Fatty acids are broken down by **beta oxidation** and yield acetyl CoA
  - An oxidized gram of fat produces more than twice as much ATP as an oxidized gram of carbohydrate

Biosynthesis (Anabolic Pathways)

- Food provides not only energy, but the carbon skeletons needed to make other molecules
  - Humans can make some amino acids by modifying compounds from citric acid cycle
    - Others must be obtained in diet
- Anabolic, or biosynthetic, pathways do not generate ATP
  - They consume ATP!
- Cellular respiration releases energy
  - It does not produce it!